

AMENDMENTS TO THE CLAIMS:

This Listing of Claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. – 54. (Canceled)

55. (New) A method for screening candidate compounds for a compound that modulates untranslated region (UTR)-dependent expression of Her-2, comprising:

a. contacting a compound with a cell engineered to express a reporter protein encoded by a nucleic acid molecule comprising: (i) a first UTR comprising an upstream open reading frame (uORF), (ii) a reporter gene coding sequence, and (iii) a second UTR comprising SEQ ID NO: 1 or a fragment thereof, wherein the first UTR is upstream of the reporter gene coding sequence and the second UTR is downstream of the reporter gene coding sequence, and wherein the nucleic acid molecule does not comprise the Her-2 3' UTR; and

b. detecting the amount or activity of the reporter protein, wherein a change in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of the reporter protein in the absence of the compound indicates that the compound modulates UTR-dependent expression of Her-2.

56. (New) A method for screening candidate compounds for a compound that modulates UTR-dependent expression of Her-2, comprising:

a. contacting a compound with a composition comprising a lysate or cell extract and a nucleic acid molecule that comprises: (i) a first UTR comprising an uORF, (ii) a reporter gene coding sequence, and (iii) a second UTR comprising SEQ ID NO: 1 or a fragment thereof, or a nucleotide sequence encoded by SEQ ID NO: 1 or a fragment thereof, wherein the first UTR is upstream of the reporter gene coding sequence and the second UTR is downstream of the reporter gene coding sequence, and wherein the nucleic acid molecule does not comprise the Her-2 3' UTR or a nucleotide sequence encoded by the Her-2 3' UTR; and

b. detecting the amount or activity of a reporter protein encoded by the nucleic acid molecule, wherein a change in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of the reporter protein in the

absence of the compound indicates that the compound modulates UTR-dependent expression of Her-2.

57. (New) A method for screening candidate compounds for a compound that reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF, comprising:

a. contacting a compound with a cell engineered to express a reporter protein encoded by a nucleic acid molecule comprising: (i) a first UTR comprising an uORF, (ii) a reporter gene coding sequence, and (iii) a second UTR comprising SEQ ID NO: 1 or a fragment thereof, wherein the first UTR is upstream of the reporter gene coding sequence and the second UTR is downstream of the reporter gene coding sequence, and wherein the nucleic acid molecule does not comprise the Her-2 3'-UTR; and

b. detecting the amount or activity of the reporter protein, wherein a decrease in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of the reporter protein in the absence of the compound indicates that the compound reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF.

58. (New) A method for screening candidate compounds for a compound that reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF, comprising:

a. contacting a compound with a composition comprising a lysate or cell extract and a nucleic acid molecule that comprises: (i) a first UTR comprising an uORF, (ii) a reporter gene coding sequence, and (iii) a second UTR comprising SEQ ID NO: 1 or a fragment thereof, or a nucleotide sequence encoded by SEQ ID NO: 1 or a fragment thereof, wherein the first UTR is upstream of the reporter gene coding sequence and the second UTR is downstream of the reporter gene coding sequence, and wherein the nucleic acid molecule does not comprise the Her-2 3' UTR, or a nucleotide sequence encoded by the Her-2 3' UTR; and

b. detecting the amount or activity of a reporter protein encoded by the nucleic acid molecule, wherein a decrease in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of the reporter protein in the absence of the compound indicates that the compound reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF.

59. (New) A method for screening candidate compounds for a compound that specifically reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF, comprising:

- a. contacting a compound with a first cell engineered to express a first reporter protein encoded by a first nucleic acid molecule comprising: (i) a first UTR comprising an uORF, (ii) a first reporter gene coding sequence, and (iii) a second UTR comprising SEQ ID NO: 1 or a fragment thereof, wherein the first UTR is upstream of the first reporter gene coding sequence and the second UTR is downstream of the first reporter gene coding sequence, and wherein the nucleic acid molecule does not comprise the Her-2 3'-UTR; and
- b. contacting the compound with a second cell engineered to express a second reporter protein encoded by a second nucleic acid molecule comprising: (i) a third UTR comprising an uORF, wherein the third UTR is identical to the first UTR, (ii) a second reporter gene coding sequence, and (iii) a fourth UTR, wherein the third UTR is upstream of the second reporter gene coding sequence and the fourth UTR is downstream of the second reporter gene coding sequence, and wherein the second nucleic acid molecule lacks SEQ ID NO: 1 or a fragment thereof;
- c. detecting the amount or activity of the first and second reporter proteins; and
- d. comparing the amount or activity of the first reporter protein with the amount or activity of the second reporter protein, wherein a decrease in the amount or activity of the first reporter protein in the presence of the compound relative to the amount or activity of the first reporter protein in the absence of the compound and no change in the amount or activity of the second reporter protein in the presence of the compound relative to the amount or activity of the second reporter protein in the absence of the compound indicates that the compound specifically reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF.

60. (New) A method for screening candidate compounds for a compound that specifically reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF, comprising:

- a. contacting a compound with a first composition comprising a lysate or cell extract and a first nucleic acid molecule that comprises: (i) a first UTR comprising an uORF, (ii) a first reporter gene coding sequence, and (iii) a second UTR comprising SEQ ID NO: 1 or a fragment thereof, or a nucleotide sequence encoded by SEQ ID NO: 1 or a

fragment thereof, wherein the first UTR is upstream of the reporter gene coding sequence and the second UTR is downstream of the first reporter gene coding sequence, and wherein the first nucleic acid molecule does not comprise the Her-2 3' UTR, or a nucleotide sequence encoded by the Her-2 3' UTR; and

b. contacting a compound with a second composition comprising a lysate or cell extract and a second nucleic acid molecule that comprises: (i) a third UTR comprising an uORF, wherein the third UTR is identical to the first UTR, (ii) a second reporter gene coding sequence, and (iii) a fourth UTR, wherein the third UTR is upstream of the second reporter gene coding sequence and the fourth UTR is downstream of the second reporter gene coding sequence, and wherein the second nucleic acid molecule lacks SEQ ID NO: 1 or a fragment thereof; and

c. detecting the amount or activity of a first reporter protein encoded by the first reporter gene coding sequence and a second reporter protein encoded by a second reporter gene coding sequence; and

d. comparing the amount or activity of the first reporter protein with the amount or activity of the second reporter protein, wherein a decrease in the amount or activity of the first reporter protein in the presence of the compound relative to the amount or activity of the first reporter protein in the absence of the compound and no change in the amount or activity of the second reporter protein in the presence of the compound relative to the amount or activity of the second reporter protein in the absence of the compound indicates that the compound specifically reduces or inhibits the ability of the Her-2 3' UTR to override the translational repression of an uORF.

61. (New) The method of claim 55, wherein a decrease in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of the reporter protein in the absence of the compound indicates that the compound inhibits or reduces the UTR-dependent expression of Her-2.

62. (New) The method of claim 56, wherein a decrease in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of the reporter protein in the absence of the compound indicates that the compound inhibits or reduces the UTR-dependent expression of Her-2.

63. (New) The method of claim 55, wherein an increase in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of

the reporter protein in the absence of the compound indicates that the compound increases the UTR-dependent expression of Her-2.

64. (New) The method of claim 56, wherein an increase in the amount or activity of the reporter protein in the presence of the compound relative to the amount or activity of the reporter protein in the absence of the compound indicates that the compound increases the UTR-dependent expression of Her-2.

65. (New) The method of claim 55, wherein the uORF is the uORF found in the Her-2 5' UTR.

66. (New) The method of claim 56, wherein the uORF is the uORF found in the Her-2 5' UTR.

67. (New) The method of claim 55, wherein the first UTR is the Her-2 5' UTR.

68. (New) The method of claim 56, wherein the first UTR is the Her-2 5' UTR.

69. (New) The method of claim 55, wherein the uORF is a Ship-2 uORF.

70. (New) The method of claim 56, wherein the uORF is a Ship-2 uORF.

71. (New) The method of claim 55, wherein the cell is a Her-2 expressing cell.

72. (New) The method of claim 55, wherein the cell is a cancer cell.

73. (New) The method of claim 55, wherein the cell is a breast cancer cell.

74. (New) The method of claim 55, wherein the cell is a SKBR-3 cell, MCF-7 cell, or BT474 cell.

75. (New) The method of claim 56, wherein the lysate is a reticulocyte lysate.

76. (New) The method of claim 56, wherein the cell extract is from a cancer cell.

77. (New) The method of claim 56, wherein the cell extract is from a SKBR-3 cell, MCF-7 cell, or BT474 cell.

78. (New) The method of claim 55, wherein the reporter protein is luciferase, neo, GUS, neomycin phosphotransferase II, β -glucuronidase, β -lactamase, tyrosinase, or α -galactosidase.

79. (New) The method of claim 56, wherein the reporter protein is luciferase, neo, GUS, neomycin phosphotransferase II, β -glucuronidase, β -lactamase, tyrosinase, or α -galactosidase.

80. (New) The method of claim 67, wherein the Her-2 5' UTR has the nucleotide sequence of SEQ ID NO: 6.

81. (New) The method of claim 68, wherein the Her-2 5' UTR has the nucleotide sequence of SEQ ID NO: 6.

82. (New) The method of claim 55, wherein the Her-2 3' UTR has the nucleotide sequence of SEQ ID NO: 3 or SEQ ID NO: 4.

83. (New) The method of claim 56, wherein the Her-2 3' UTR has the nucleotide sequence of SEQ ID NO: 3 or SEQ ID NO: 4.

84. (New) The method of claim 57, wherein the uORF is the uORF found in the Her-2 5' UTR.

85. (New) The method of claim 58, wherein the uORF is the uORF found in the Her-2 5' UTR.

86. (New) The method of claim 57, wherein the first UTR is the Her-2 5' UTR.

87. (New) The method of claim 58, wherein the first UTR is the Her-2 5' UTR.

88. (New) The method of claim 57, wherein the uORF is a Ship-2 uORF.

89. (New) The method of claim 58, wherein the uORF is a Ship-2 uORF.

90. (New) The method of claim 57, wherein the cell is a Her-2 expressing cell.

91. (New) The method of claim 57, wherein the cell is a cancer cell.

92. (New) The method of claim 57, wherein the cell is a breast cancer cell.

93. (New) The method of claim 57, wherein the cell is a SKBR-3 cell, MCF-7 cell, or BT474 cell.

94. (New) The method of claim 58, wherein the lysate is a reticulocyte lysate.

95. (New) The method of claim 58, wherein the cell extract is from a cancer cell.

96. (New) The method of claim 58, wherein the cell extract is from a SKBR-3 cell, MCF-7 cell, or BT474 cell.

97. (New) The method of claim 57, wherein the reporter protein is luciferase, neo, GUS, neomycin phosphotransferase II, β -glucuronidase, β -lactamase, tyrosinase, or α -galactosidase.

98. (New) The method of claim 58, wherein the reporter protein is luciferase, neo, GUS, neomycin phosphotransferase II, β -glucuronidase, β -lactamase, tyrosinase, or α -galactosidase.

99. (New) The method of claim 86, wherein the Her-2 5' UTR has the nucleotide sequence of SEQ ID NO: 6.

100. (New) The method of claim 87, wherein the Her-2 5' UTR has the nucleotide sequence of SEQ ID NO: 6.

101. (New) The method of claim 57, wherein the Her-2 3' UTR has the nucleotide sequence of SEQ ID NO: 3 or SEQ ID NO: 4.

102. (New) The method of claim 58, wherein the Her-2 3' UTR has the nucleotide sequence of SEQ ID NO: 3 or SEQ ID NO: 4.

103. (New) The method of claim 59, wherein the uORF is the uORF found in the Her-2 5' UTR.

104. (New) The method of claim 60, wherein the uORF is the uORF found in the Her-2 5' UTR.

105. (New) The method of claim 59, wherein the first and the third UTR is the Her-2 5' UTR.

106. (New) The method of claim 60, wherein the first and the third UTR is the Her-2 5' UTR.

107. (New) The method of claim 59, wherein the uORF is a Ship-2 uORF.

108. (New) The method of claim 60, wherein the uORF is a Ship-2 uORF.

109. (New) The method of claim 59, wherein the first and second cells are cancer cells.

110. (New) The method of claim 59, wherein the first and second cells are breast cancer cells.

111. (New) The method of claim 60, wherein the cell extract is from a cancer cell.